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POST-VACCINATION IMMUNITY TO MEASLES IN CHILDREN WITH DIFFERENT CLINICAL MANIFESTATIONS OF POST-COVID SYNDROME

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Abstract. The state of post-vaccination immunity to measles was studied in 129 previously vaccinated children with various manifestations of post-COVID syndrome—namely, long COVID (lasting 4 to 12 weeks) and chronic post-COVID syndrome (CPCS, lasting 12 weeks or more). **Materials and methods.**The study involved children aged 1 to 12 years who had previously suffered from COVID-19 and experienced frequent episodes of bronchopneumonia. **Results.**Persistent clinical symptoms following acute coronavirus infection (after the fourth week) negatively affected the titers of anti-measles antibodies (Abs). This explains the high frequency of seronegative patients for measles among those with post-COVID syndrome. Prolonged clinical symptom manifestation in different variants of post-COVID syndrome led to a decrease in measles antibody titers ($r = –0.6105$, $p < 0.001$), while IgG antibodies to SARS-CoV-2 declined over time, which is confirmed by a statistically significant inverse correlation ($r = –1$, $p < 0.001$). **Conclusion.**The clinical course of recurrent bronchopneumonia in CPCS was more severe compared to that in long COVID cases.

Keywords: post-vaccination immunity to measles, clinical post-covid syndrome, children

Actuality. Post-COVID syndrome in children is a pressing issue in modern medicine that demands the attention of specialists across various medical fields [1–5].

Recent literature has highlighted the specific characteristics of post-COVID syndrome in children, including multi-organ involvement, autoimmune damage, and pronounced changes in immune system function [6–8].

The rising incidence of measles, pertussis, and hospitalizations due to community-acquired pneumonia among children previously infected with COVID-19, along with the detection of low antibody titers to vaccine-preventable infections and the growing number of children diagnosed with autoimmune systemic diseases and secondary immunodeficiencies, provides a rationale for further investigation into this problem [9–15].

All of these factors underscore the relevance of this research topic and compel pediatricians to pay closer attention to this specific group of children [17–19].

Research Objective: To study the clinical features of bronchopneumonia and the state of post-vaccination immunity to measles in previously vaccinated children with different forms of post-COVID syndrome.

Materials and Methods: A total of 129 children aged 1 to 12 years who had previously contracted COVID-19 were observed. All children had been vaccinated against measles with the Measles Attenuated Vaccine (Serum Institute of India Pvt. Ltd., 212/2 Hadapsar, Pune 411028, India; Batch No: (01)08901213041928) and the MMR Vaccine (Measles, Mumps, Rubella) (Serum Institute of India Pvt. Ltd., Batch No: 0164W001).

The diagnosis of post-COVID syndrome was made based on the International Classification of Diseases (ICD-10), using code U09.9 — "Post COVID-19 condition, unspecified," which also encompasses post-COVID states. Depending on the duration of symptoms, the condition was classified into two categories:

Long COVID — clinical manifestations persisting for more than 4 weeks but less than 12 weeks from the onset of illness, observed in 61 patients (47.3%).

Chronic COVID or Post-COVID Syndrome (PCS) — clinical manifestations lasting beyond 12 weeks from the onset of the disease, observed in 68 patients (52.7%).

Clinical and laboratory examinations, diagnostics, and treatment of the patients were carried out in accordance with the current clinical protocol for diagnosis and treatment approved by the Ministry of Health of the Republic of Uzbekistan [7].

A history of previous COVID-19 infection was confirmed through the detection of antibodies to S-RBD SARS-CoV-2 IgG using the ELISA-BEST (Novosibirsk) test for COVID-19 (neutralizing S antibodies). Antibody titers above 1 ME/ml were considered positive.

Measles antibody titers were determined using the *Vector Measles-IgG ELISA* (Novosibirsk) for quantitative measurement in blood serum. The interpretation of values was as follows:

Below 0.12 ME/ml – negative or seronegative, Between 0.13 and 0.17 ME/ml – weakly positive, Above 0.18 ME/ml – considered positive, indicating high measles antibody titers.

All children in both the **long COVID and PCS** (Post-COVID Syndrome) groups were further subdivided into seronegative and **seropositive categories** based on their antibody titers. One of the predominant pathologies observed in post-COVID syndrome was recurrent bronchopneumonia of varying severity.

The collected data were statistically analyzed using methods of variation statistics, including the calculation of arithmetic means (M), standard errors of the mean (m), confidence intervals (σ), and statistically significant differences determined by Student's t-test.

Research results. Post-COVID syndrome in children manifested in various forms. These included frequent inflammatory diseases of the upper and lower respiratory tract (such as sinusitis, maxillary sinusitis, otitis, bronchitis, bronchiolitis, and bronchopneumonia), systemic connective tissue diseases (such as arthritis and polyarthritis), neurological conditions (such as polyradiculoneuritis, encephalopathies, and brain cysts), as well as various vasculitides, and involvement of the urinary system, kidneys, and gastrointestinal tract [6–7].

One of the most predominant pathologies associated with post-COVID syndrome was bronchopneumonia of varying severity. In this regard, we studied the clinical course of bronchopneumonia in children with different variants of post-COVID syndrome (see Table 1).

Signs of extremely severe conditions, such as central cyanosis and severe respiratory failure (notable by head-nodding movements during breathing), were significantly more common in patients with chronic post-COVID syndrome (CPCS) ($p < 0.01$). Although subcostal retraction during breathing is recognized by the World Health Organization as a reliable clinical indicator, it was significantly more frequent in children with long COVID—38 cases (70.3%)—compared to only 7 cases (20.5%) in the CPCS group ($p < 0.001$).

High fever (up to 39–40°C), weakness, excessive sweating, drowsiness, body aches, and chest pain were observed with similar frequency in both long COVID and CPCS groups ($p > 0.05$). Hypothermia (body temperature of 35°C or lower) was more characteristic of CPCS—8 children (23.5%)—versus only 1 child (1.8%) with long COVID ($p < 0.001$). This may be related to toxic damage to the central nervous system and the presence of TORCH infections such as cytomegalovirus (CMV), herpes simplex virus types 1 and 2 (HSV-1,2), and concurrent bacterial infections.

Dry cough was more typical at the onset of recurrent bronchopneumonia episodes in children with long COVID, whereas wet cough and pulmonary crepitations were more characteristic of CPCS ($p < 0.05$; $p < 0.001$). Severe dyspnea was more frequently observed in the long COVID group ($p < 0.001$), whereas tachycardia and excessive sweating were significantly more common in the CPCS group ($p < 0.001$; $p < 0.05$).

Our analysis showed that 16 children (47%) with CPCS were diagnosed with interstitial bronchopneumonia, compared to only 8 children (14.8%) in the long COVID group ($p < 0.001$). Complications were also observed

more frequently in CPCS patients; however, these differences were not statistically significant ($p < 0.05$).

Table 1

Features of the clinical course of bronchopneumonia in children with post-covid syndrome

	Symptoms	Long-covid n=54	CPCS n=34	Reliability P
1.	Central cyanosis	1/1,8	10/29,4	˂0,01
2.	Severe respiratory failure (nodding movements)	1/1,8	10/29,4	˂0,01
3.	Retraction of the hypochondria during breathing	38/70,3	7/20,5	˂0,001
3.	Increased body temperature	48/88,8	32/94,1	˃0,05
4.	Decrease in temperature to 35°C and below	1/1,8	8/23,5	˂0,01
5.	Cough: dry	24/44,4	6/17,6	˂0,05
	Wet	30/55,5	28/82,3	˂0,01
6.	Auscultation: harsh breathing	15/27,7	34/100	˂0,001
	dry wheezing	20/37	34/100	˂0,001
	wet wheezing	30/55,5	34/100	˂0,001
	crepitation	6/11,1	7/20,5	˃0,05
	weakened breathing	23/42,5	30/88,2	˂0,01
7.	Shortness of breath: rapid breathing	38/70,3	14/41,1	˂0,01
8.	Increased heart rate	15/27,7	24/70,5	˂0,001
9.	Percussion: pulmonary sound	-	-	
	Dullness	23/42,5	30/88,2	˂0,01
	Box sound	23/42,5	19/55,8	˃0,05
9.	Increased sweating	38/70,3	34/100	˂0,05
10.	Weakness, drowsiness	52/96,2	33/97,0	˃0,05
11.	Body aches, chest pain	45/83,3	33/97,0	˃0,05
12.	Loss of appetite	46/85,1	34/100	˂0,05
13.	Severe course	23/42,5	32/100	˂0,001
14.	Moderate-severe	28/51,8	2/5,8	˂0,001
15.	Mild	-	-	
16.	Segmental pneumonia or polysegmental	28/51,8	10/29,4	˂0,001

17.	Lobar pneumonia	4/7,4	2/5,8	˃0,05
18.	Focal pneumonia or focal-confluent	13/24	1 /2,9	˃0,05
19.	Croupous pneumonia	1/1,8	5/ 14,7	˃0,05
20.	Interstitial pneumonia	8/14,8	16/47,0	˂0,001
21.	Complications: pleural; pulmonary complications - cystic lesions, abscess	1/1,8	6/17,6	˃0,05

The geometric mean titers of IgG antibodies to SARS-CoV-2 and measles IgG in children with long COVID syndrome (expressed in ME/ml) were subsequently analyzed, and the data are presented in Table 2.
A comparative analysis was conducted between children with seronegative measles antibody titers and those who were seropositive for IgG SARS-CoV-2, as well as between measles-seropositive children and their corresponding SARS-CoV-2 IgG antibody titers. Among patients with seronegative measles IgG titers, very high levels of IgG SARS-CoV-2 antibodies were observed, ranging from 5.01 to 8.63 ME/ml. Children with protective antibody titers against measles also demonstrated elevated levels of IgG SARS-CoV-2 antibodies, ranging from 1.64 to 16.0 ME/ml.
Correlation analysis between these two groups revealed that the higher the IgG SARS-CoV-2 antibody titers, the lower the measles IgG antibody titers. In the seronegative group, this correlation was not statistically significant ($r = 0$, $p > 0.05$); however, in the seropositive group, the inverse correlation was statistically significant ($r = -1$, $p < 0.01$).

Table 2

Geometric mean titers of IgG SARS-COV-2 and IgG antibodies to measles in children with bronchopneumonia with Long-covid syndrome (ME/ml).

Indicators	seronegative patients		seropositive patients	
	Sero + Anti-IgG SARS-COV-2 antibody n=18	Sero - AT IgG to measles n=18	grey+ IgG SARS-COV-2 n=43	Ser+ AT IgG to measles n=43
	1	2	3	4
1.	7,1±0,8	0,02±0,9	7,73±0,5	2,2±0,5
2. Limit of oscillations	5,01-8,63	0,01-0,14	1,64-16,0	0,18-1,98
3.	r=0		r=-1; P˂0,01	

Correlations –r between AT to IgG SARS-COV-2 and AT IgG to measles				

Note: *- reliability between AT IgG 1-3 and 2-4; correlations between 1-2 and 3-4

The geometric mean titers of IgG antibodies to SARS-CoV-2 and measles IgG in children with chronic post-COVID syndrome (CPCS), expressed in ME/ml, are presented in Table 3.

Among seronegative patients with CPCS, the IgG SARS-CoV-2 antibody level was 5.8 ± 0.1 ME/ml, with a range from 7.83 to 16 ME/ml, while the IgG antibody titer to measles was 0.011 ± 0.0002 ME/ml, with a range from 0.01 to 0.06 ME/ml.

In the group of seropositive patients for measles, IgG SARS-CoV-2 antibody titers were 8.2 ± 3.7 ME/ml, ranging from 4.75 to 12.4 ME/ml, and measles antibody titers were high in 54 patients—0.93 ± 0.007 ME/ml, with a range from 0.23 to 2.1 ME/ml (see Table 3).

The conducted correlation analysis between IgG SARS-CoV-2 antibody values and measles IgG titers revealed an inverse proportional relationship in the group of measles-seropositive children with statistically significant indicators ($r = –0.991$; $p < 0.01$). In the seronegative group, however, the correlation was not statistically significant ($r = 0$; $p > 0.05$).

Table 3

Geometric mean titers of IgG SARS-COV-2 and IgG antibodies to measles in children with bronchopneumonia in chronic respiratory failure (IU/ml)

Indicators	measles seronegative patients		measles seropositive patients	
	AT to IgG SARS-COV-2 n=14	Sero- AT IgG to measles n=14	IGG SARS-SOV-2 n=54	Sero+ AT IgG to measles n=54
	1	2	3	4
1.	5,8±0,1	0,011±0,0002	8,2±3,7	0,93±0,007
2. Limit of oscillations	7,83-16	0,01-0,06	4,75-12,4	0,23-2,1
3. Correlations –r	r=0 p˃0,05		r=-0,991; p˂0,01	

between AT to IgG SARS-COV-2 and AT IgG to measles				

Note: *- reliability between AT IgG 1-3 and 2-4; correlations between 1-2 and 3-4

A correlation analysis was conducted between IgG SARS-CoV-2 antibody levels and measles antibody titers in both seronegative and seropositive patient groups with long COVID and CPCS (Table 4).
The results of the study revealed that prolonged clinical symptom manifestation in post-COVID syndrome leads to a decrease in measles antibody titers ($r = –0.6105$, $p < 0.001$). Additionally, IgG SARS-CoV-2 antibody levels also decline over time, as evidenced by a statistically significant inverse correlation ($r = –1$, $p < 0.001$).

Table 3

Correlation relationships between the indicators of AT to IgG SARS-COV-2 and AT to IgG measles in groups of seropositive and seronegative patients to measles with different variants of post-COVID syndrome

Indicators	measles seropositive patients		measles seronegative patients	
	↑AT to IgG SARS-COV-2 n=42	AT to IgG measles (sero+) n=42	↑AT to IgG SARS-COV-2 n=14	AT to measles IgG (sero-) n=14
Correlations between Long-covid and HPS	r=-1, p˂0,001	r=-0,6105, p˂0,001	r=0, p˃0,05	r=0, p˃0,05

The study demonstrated that in both long COVID and CPCS (chronic post-COVID syndrome), elevated titers of antibodies to COVID-19 were inversely correlated with measles antibody levels. This finding supports the conclusion that persistent clinical symptoms following acute COVID-19 infection—beginning after the fourth week, and especially from the fifth to the twelfth week and beyond—have a negative impact on measles antibody titers. This explains the high frequency of measles-seronegative patients in the CPCS group.
Prolonged manifestation of clinical symptoms in post-COVID syndrome leads to a reduction in measles antibody titers ($r = –0.6105$, $p < 0.001$), while IgG SARS-CoV-2 antibody levels also decline over time, with a statistically significant inverse correlation ($r = –1$, $p < 0.001$) (Table 3).
In children with long COVID, bronchopneumonia typically presented as a moderately severe illness, often accompanied by dyspnea, subcostal

retractions during breathing, and frequently diagnosed as segmental bronchopneumonia. In contrast, CPCS was associated with a higher incidence of severe bronchopneumonia, central cyanosis, severe respiratory failure (including head-nodding breathing), and pronounced signs of central nervous system intoxication such as hypothermia (body temperature of 35°C or below) and increased pulse rate. Interstitial pneumonia was also commonly diagnosed in this group.

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